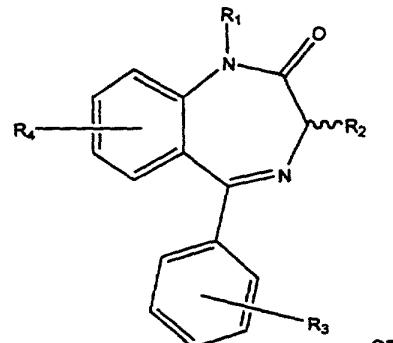


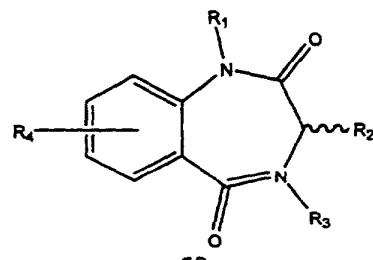
CLAIMS

We claim:

1. A method of treating a condition associated with dysregulation of the process of cell death in a subject, comprising administering to the subject an effective amount of a benzodiazepine compound.
- 5
2. The method of claim 1, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.
- 10
3. The method of claims 1 or 2, wherein the benzodiazepine induces apoptosis in a low serum assay.
- 15
4. The method of claim 1, wherein the condition is not a chronic inflammatory condition.
5. The method of claim 1, wherein the benzodiazepine is a compound having the structure:



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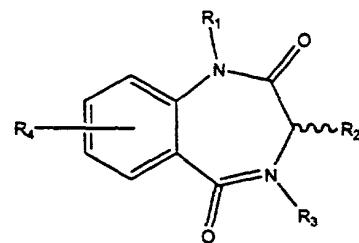
- or its enantiomer,
wherein,
R₁ is aliphatic or aryl;
R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in
5 hydrogen bond formation,
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
and
each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino,
10 lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having
1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;
or a pharmaceutically acceptable salt, prodrug or derivative thereof.
6. The method of claim 1, wherein the benzodiazepine is a compound having the
15 structure:
-
- or its enantiomer,
wherein,
R₁ is aliphatic or aryl;
R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in
20 hydrogen bond formation,
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic,
and

PCT/EP2010/062450

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic; or a pharmaceutically acceptable salt, prodrug or derivative thereof.

5

7. The method of claim 1, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

10 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

15 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

20 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

8. The method of claim 1, wherein the cell death is apoptotic.

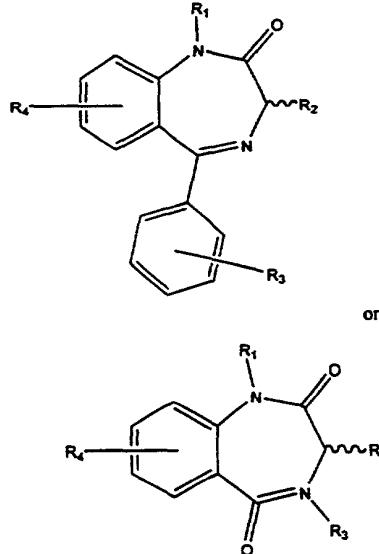
9. The method of claim 1, wherein the cell death is necrotic.

25

10. The method of claim 1, wherein the dysregulation of the process of cells death is caused by disruption of the FAS pathway.

11. The method of claim 1, wherein the condition is an autoimmune disease.
12. The method of claim 11, wherein the autoimmune disease is a disease selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis,
5 Sjögren's syndrome, graft-versus-host disease and myasthenia gravis.
13. The method of claim 1, wherein the condition is a chronic inflammatory condition.
14. The method of claim 11, wherein the chronic inflammatory condition is psoriasis,
10 asthma, or Crohn's disease.
15. The method of claim 1, wherein the condition is a hyper-proliferative disorder.
16. The method of claim 15, wherein the hyperproliferative disorder is a neoplastic
15 condition.
17. The method of claim 15, wherein the hyperproliferative disorder is selected from the group consisting of B-cell lymphoma, T-cell lymphoma, cancer, chemo-resistant cancers, disorders related to deficient p53 expression, and disorders related to
20 overexpression of endogenous bcl-x_L.
18. The method of claim 1, wherein the condition is induced by a viral infection.
19. The method of claim 16, wherein the viral infection is caused by a virus selected
25 from the group consisting of herpes virus, papilloma virus and Human Immunodeficiency Virus (HIV).
20. The method of claim 1, wherein the condition is atherosclerosis or osteoarthritis.
- 30 21. The method of claim 1, further comprising co-administering one or more additional agents to the subject.

- PCT/EP2002/002650
22. The method of claim 21, wherein the additional agent is a chemotherapeutic agent or radiation.
23. The method of claim 1, wherein the compound is administered orally, parenterally, 5 topically or intranasally.
24. A method of treating an autoimmune disease in a subject comprising administering to the subject an effective amount of a benzodiazepine compound.
- 10 25. The method of claim 24, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.
- 15 26. The method of claims 24 or 25, wherein the benzodiazepine induces apoptosis in a low serum assay.
27. The method of claim 24, wherein the benzodiazepine is a compound having the structure:



20 or its enantiomer,
wherein,
R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;

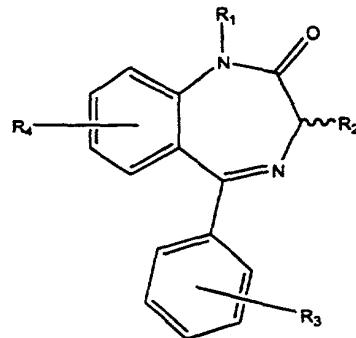
5 and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

10

28. The method of claim 24, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

15 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

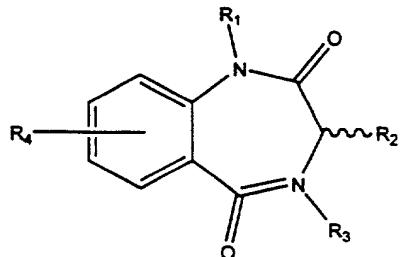
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

20 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

25 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

29. The method of claim 24, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

5 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R, or -R₆-C(=O)-NH-R₇,

10 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

15 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

30. The method of claim 24, wherein the autoimmune disease is a disease selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, graft-versus-host disease and myasthenia gravis.

20

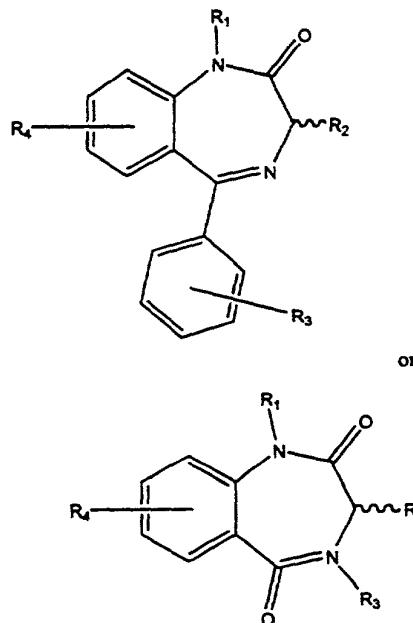
31. The method of claim 24, further comprising co-administering one or more additional agents to the subject.

32. The method of claim 31, wherein the additional agent is an immunosuppressant.

25

33. A method of treating a chronic inflammatory condition in a subject comprising administering to the subject an effective amount of a benzodiazepine compound.

- PCT/US2007/035360
34. The method of claim 33, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.
- 5 35. The method of claims 33 or 34, wherein the benzodiazepine induces apoptosis in a low serum assay.
36. The method of claim 33, wherein the benzodiazepine is a compound having the structure:



10

or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

15 R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

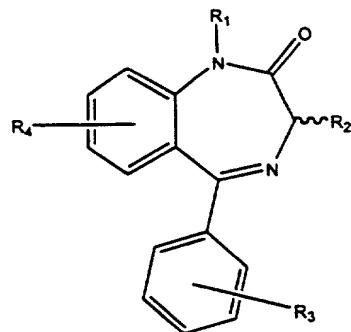
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino,

20 lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

37. The method of claim 33, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in
10 hydrogen bond formation,

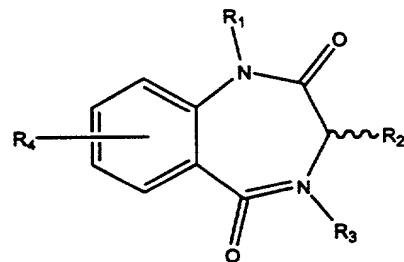
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino,
15 lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having
1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

38. The method of claim 33, wherein the benzodiazepine is a compound having the
20 structure:



or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

5 wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having

10 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

39. The method of claim 33, wherein the chronic inflammatory condition is psoriasis, asthma, or Crohn's disease.

15

40. The method of claim 33, further comprising co-administering one or more additional agents to the subject.

41. The method of claim 40, wherein the additional agent is an anti-inflammatory agent.

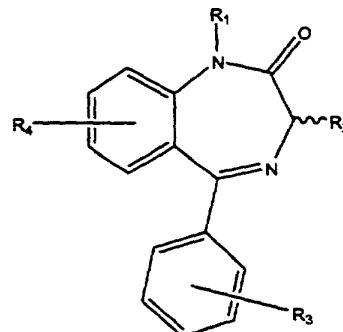
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42. A method of treating a hyperproliferative disorder in a subject comprising administering to the subject an effective amount of a benzodiazepine compound.

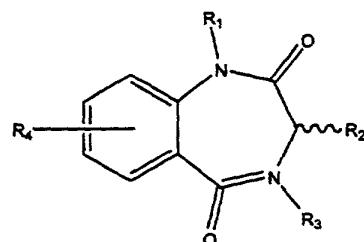
25 43. The method of claim 42, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.

44. The method of claims 42 or 43, wherein the benzodiazepine induces apoptosis in a low serum assay.

45. The method of claim 42, wherein the benzodiazepine is a compound having the structure:



or



5 or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

10 wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

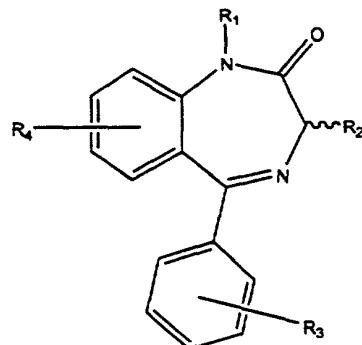
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylarnino, hydroxyarnino, an aliphatic group having

15 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

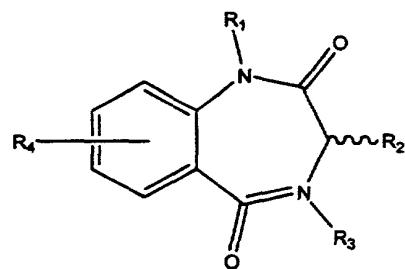
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

46. The method of claim 42, wherein the benzodiazepine is a compound having the structure:



5 or its enantiomer,
wherein,
R₁ is aliphatic or aryl;
R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in
hydrogen bond formation,
10 wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
and
each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino,
lower-alkyl-substituted-amino, acetyl amino, hydroxyamino, an aliphatic group having
15 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

47. The method of claim 42, wherein the benzodiazepine is a compound having the structure:



20 or its enantiomer,
wherein,

R, is aliphatic or aryl;

R_2 is aliphatic, aryl, $-NH_2$, $-NHC(=O)-R_5$ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

5 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

10 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

48. The method of claim 42, wherein the hyperproliferative disorder is a neoplastic condition.

15 49. The method of claim 42, wherein the hyperproliferative disorder is selected from the group consisting of B-cell lymphoma, T-cell lymphoma, cancer, chemo-resistant cancers, disorders related to deficient p53 expression, and disorders related to overexpression of endogenous bcl-x_L.

20 50. The method of claim 42, further comprising co-administering one or more additional
agents to the subject.

51. The method of claim 50, wherein at least one additional agent is a chemotherapeutic agent, or radiation.

25

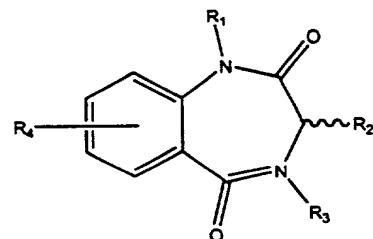
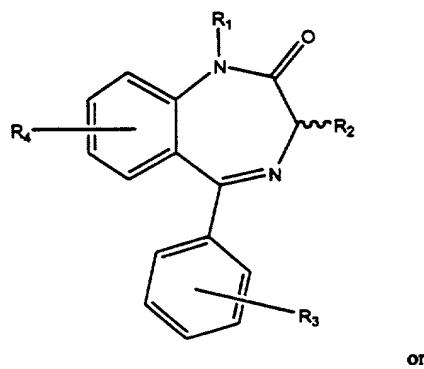
52. A method of treating a condition associated with the dysregulation of the process of cell death in a subject, comprising administering to the subject an effective amount of a benzodiazepine compound, wherein the condition is induced by a viral infection.

30

53. The method of claim 52, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.

5 54. The method of claims 52 or 53, wherein the benzodiazepine induces apoptosis in a low serum assay.

55. The method of claim 52, wherein the benzodiazepine is a compound having the structure:



10

or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

15 R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

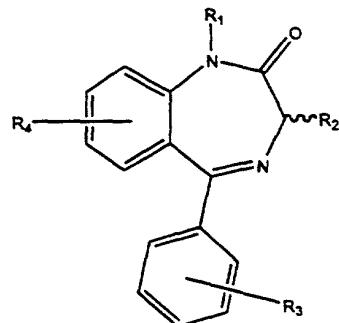
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

56. The method of claim 52, wherein the benzodiazepine is a compound having the structure:



5

or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in
10 hydrogen bond formation,

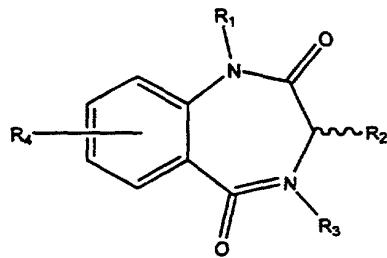
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino,
15 lower-alkyl-substituted-amino, acetyl amino, hydroxyamino, an aliphatic group having
1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

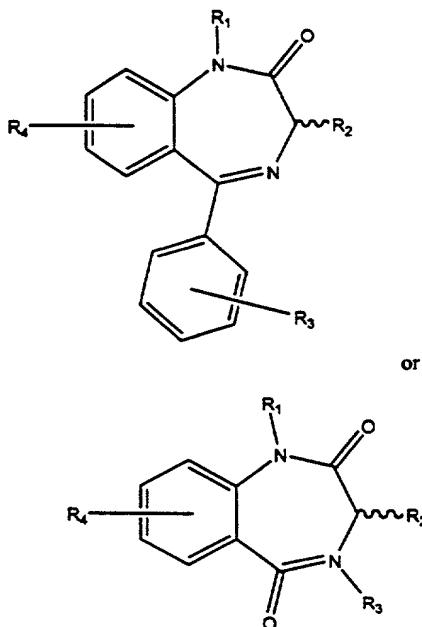
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

57. The method of claim 52, wherein the benzodiazepine is a compound having
20 the structure:



- 000000000000000000000000
- or its enantiomer,
wherein,
 R_1 is aliphatic or aryl;
 R_2 is aliphatic, aryl, $-NH_2$, $-NHC(=O)-R_5$ or a moiety that participates in
5 hydrogen bond formation,
wherein R_5 is aryl, heterocyclic, $-R_6-NH-C(=O)-R_7$ or $-R_6-C(=O)-NH-R_7$,
wherein R_6 is an aliphatic linker of 1-6 carbons and R_7 is aliphatic, aryl, or heterocyclic;
and
each of R_3 and R_4 is independently hydrogen, hydroxy, alkoxy, halo, amino,
10 lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having
1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;
or a pharmaceutically acceptable salt, prodrug or derivative thereof.
- 15 58. The method of claim 52, wherein the viral infection is caused by a virus selected
from the group consisting of herpes virus, papilloma virus and Human
Immunodeficiency Virus.
- 20 59. The method of claim 52, further comprising co-administering one or more additional
agents to the subject.
- 25 60. The method of claim 59, wherein the additional agent is an antiviral agent.
61. A method of promoting cell death comprising contacting a cell or tissue with an
effective amount of a benzodiazepine compound.
- 25 62. The method of claim 61, wherein the benzodiazepine does not bind to a central
benzodiazepine receptor and binds only with low affinity to a peripheral
benzodiazepine receptor.
- 30 63. The method of claims 61 or 62, wherein the benzodiazepine induces apoptosis in a
low serum assay.

64. The method of claim 61, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

5 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

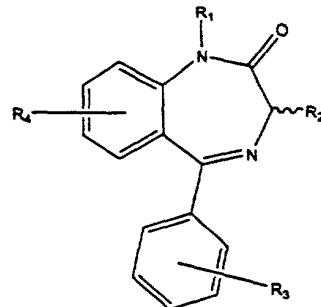
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

10 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

15 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

56. The method of claim 61, wherein the benzodiazepine is a compound having the structure:



5 or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

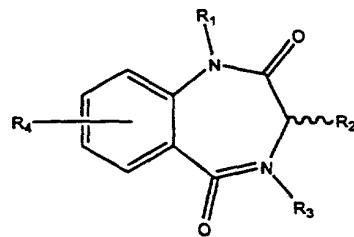
10 wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R, or -R₆-C(=O)-NH-R,,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetyl amino, hydroxyamino, an aliphatic group having 15 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

66. The method of claim 61, wherein the benzodiazepine is a compound having the structure:



20

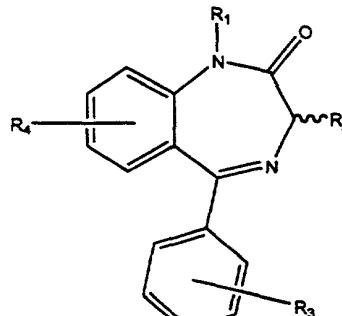
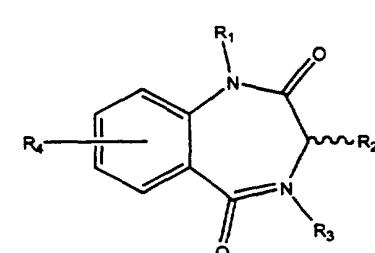
or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
5 and
each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino,
lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having
1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

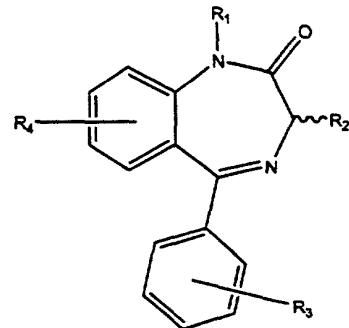
- 10 67. The method of claim 61, wherein the cell death occurs due to necrosis, apoptosis, or regulation of the FAS pathway.
- 15 68. The method of claim 61, wherein the cell is hyperproliferative.
- 16 69. The method of claim 61, wherein the cell or tissue is autoimmunogenic or is affected by autoimmune reaction.
- 20 70. The method of claim 61, wherein the cell or tissue is inflammatory or is affected by inflammation.
- 25 71. The method of claim 61, wherein the cell is a monocytic cell.
72. The method of claim 61, wherein the cell is infected with a virus.
- 26 73. The method of claim 61, further comprising co-administering one or more additional agents to the cell.
- 30 74. The method of claim 73, wherein the additional agent is selected from the group consisting of: chemotherapeutic agent, immunosuppressant, anti-inflammatory agent, antiviral agent, or radiation.

- 10
- 15
- 20
75. A method of enhancing the efficacy of an agent for treating an autoimmune disease comprising administering an effective amount of a benzodiazepine compound.
76. The method of claim 75, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.
77. The method of claims 75 or 76, wherein the benzodiazepine induces apoptosis in a low serum assay.
78. The method of claim 75, wherein the benzodiazepine is a compound having the structure:
- 
- or
- 
- or its enantiomer,
- wherein,
- R₁ is aliphatic or aryl;
- R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,
- wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
- wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;
- and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

5

79. The method of claim 75, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

10 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

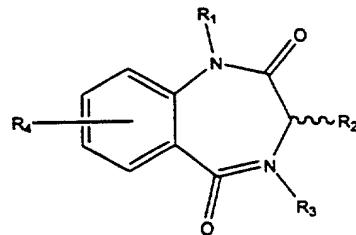
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R, or -R₆-C(=O)-NH-R₇,

15 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

20 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

80. The method of claim 75, wherein the benzodiazepine is a compound having the structure:



5 or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

10 wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 15 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

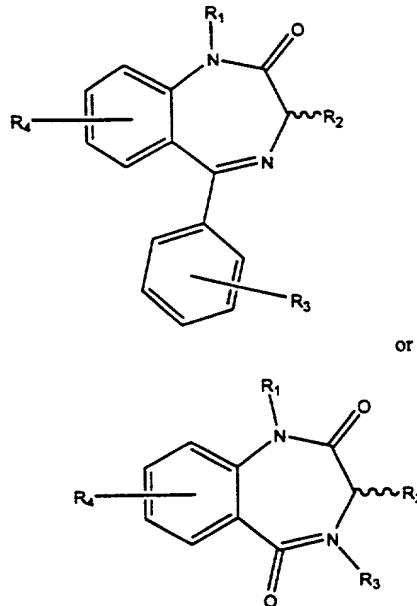
81. A method of inhibiting viral proliferation in a virally infected cell comprising contacting the cell with an effective amount of one or more benzodiazepine 20 compounds.

82. The method of claim 81, wherein the benzodiazepine does not bind to a central benzodiazepine receptor and binds only with low affinity to a peripheral benzodiazepine receptor.

25

83. The method of claims 81 or 82, wherein the benzodiazepine induces apoptosis in a low serum assay.

84. The method of claim 81, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

5 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

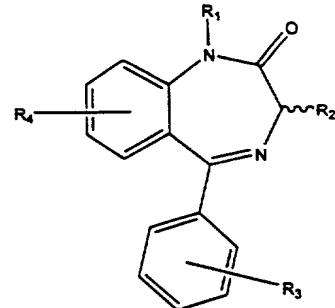
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

10 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetyl amino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

15 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

85. The method of claim 81, wherein the benzodiazepine is a compound having the structure:



5 or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

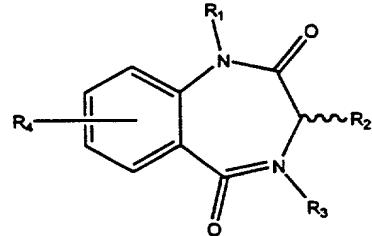
10 wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetyl amino, hydroxyamino, an aliphatic group having 15 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

86. The method of claim 81, wherein the benzodiazepine is a compound having the structure:



20

or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; 5 and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

10

87. The method of claim 81, wherein the viral infection is caused by a virus selected from the group consisting of herpes virus, hepatitis virus, or a retrovirus.

15

88. The method of claim 87, wherein the virus is selected from the group consisting of: HSV-1, HSV-2, HCMV, HBV, HCV, or HIV.

20

89. A method of identifying agents useful to treat a condition associated with a process of cell death in a subject, wherein the method comprises contacting a cell maintained in low serum media with a test agent under conditions that induce cell death, and assaying for cell death, thereby identifying agents useful to treat the condition associated with the process of cell death.

25

90. The method of claim 89, further comprising determining whether the test agent binds to a central benzodiazepine receptor or binds with low affinity to a peripheral benzodiazepine receptor.

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91. The method of claim 89, wherein the process of cell death is necrotic.

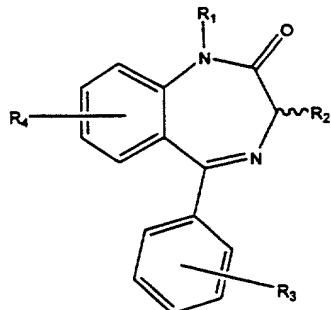
92. The method of claim 89, wherein the process of cell death is apoptotic.

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93. The method of claim 89, wherein the cell is selected from the group of cells consisting of: autoimmunogenic cell, inflammatory cell, hyperproliferative cell, virally-infected cell, atherosclerotic cell or ostearthritic cell.
- 5 94. The method of claim 89, wherein the cell is a cell affected by an autoimmune condition or a cell affected by an inflammatory condition.
- 10 95. The method of claim 89, further comprising contacting a control cell maintained in low serum media with a benzodiazepine compound under conditions that induce cell death.
- 15 96. The method of claim 95, wherein the benzodiazepine compound has the structure:
- or
- 15 or its enantiomer,
- wherein,
- R₁ is aliphatic or aryl;
- R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,
- wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
- 20 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic; or a pharmaceutically acceptable salt, prodrug or derivative thereof.

5

97. The method of claim 95, wherein the benzodiazepine is a compound having the structure:



or its enantiomer,

10 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

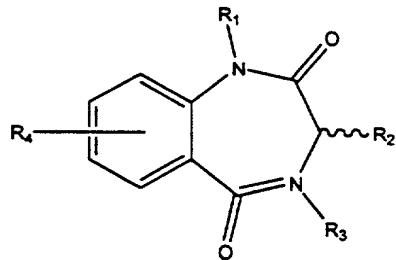
15 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

20 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

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98. The method of claim 95, wherein the benzodiazepine is a compound having the structure:



5 or its enantiomer,

wherein,

R₁ is aliphatic or aryl;

10 R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₈,

15 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetyl-amino, hydroxyamino, an aliphatic group having

15 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

99. The method of claim 91, wherein the serum level is less than or equal to about 10% by volume of the maintenance medium.

20

100. The method of claim 91, wherein the serum level is less than or equal to about 5% by volume of the maintenance medium.

25

101. The method of claim 91, wherein the serum level is less than or equal to about 1% by volume of the maintenance medium.

102. The method of claim 91, wherein the serum level is less than or equal to about 0.5% by volume of the maintenance medium.

- 103.
103. The method of claim 91, wherein the serum level is less than or equal to about 0.2% by volume of the maintenance medium.
- 5
104. The method of claim 95, wherein the benzodiazepine compound is detectably labeled.
- 10
105. Use of a benzodiazepine compound to treat a condition associated with dysregulation of the process of cell death in a subject, wherein the benzodiazepine is a compound having the structure:
- or
- or its enantiomer,
- wherein,
- R₁ is aliphatic or aryl;
- 15
- R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,
- wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,
- wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and
- 20
- each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

106. The use as in claim 105, wherein the cell death is due to necrosis, apoptosis, or regulation of the FAS pathway.

5

107. The use as in claim 105, wherein the condition is an autoimmune disease selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, graft-versus-host disease and myasthenia gravis.

10 108. The use as in claim 105, wherein the condition is a chronic inflammatory condition.

109. The use as in claim 108, wherein the inflammatory condition is psoriasis, asthma, or Crohn's disease.

15

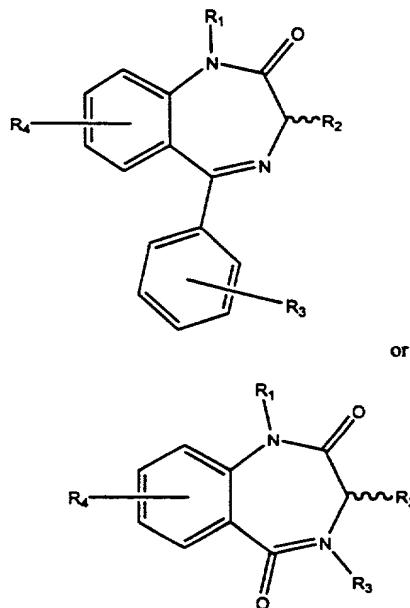
110. The use as in claim 105, wherein the condition is a hyperproliferative disorder or neoplasm.

111. The use as in claim 110, wherein the hyperproliferative disorder is selected from 20 the group consisting of B-cell lymphoma, T-cell lymphoma, cancer, chemo-resistant cancers, disorders related to deficient p53 expression, and disorders related to overexpression of endogenous bcl-x_L.

112. The use as in claim 105, wherein the condition is induced by a viral infection, 25 wherein the viral infection is caused by a virus selected from the group consisting of herpes virus, papilloma virus and Human Immunodeficiency Virus (HIV).

113. The use as in claim 105, wherein the condition is atherosclerosis or osteoarthritis.

114. A benzodiazepine compound having the structure:



or its enantiomer,

5 wherein,

R₁ is aliphatic or aryl;

10 R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

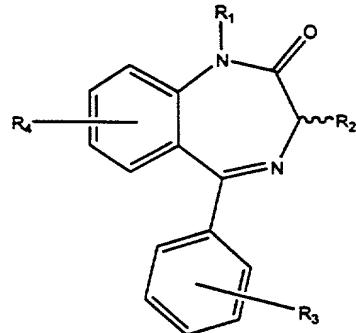
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

15 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetyl-amino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

15 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

115. A benzodiazepine compound having the structure:



or its enantiomer,

5 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

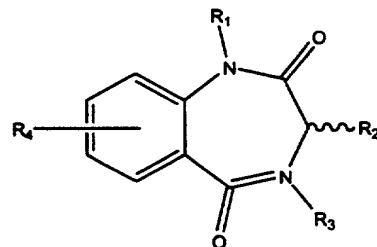
wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

10 wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic; and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

15 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

116. A benzodiazepine compound having the structure:



or its enantiomer,

20 wherein,

R₁ is aliphatic or aryl;

R₂ is aliphatic, aryl, -NH₂, -NHC(=O)-R₅ or a moiety that participates in hydrogen bond formation,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇, wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;

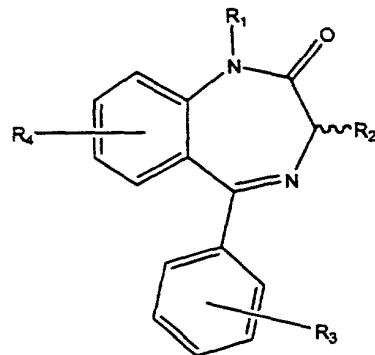
5 and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylarnino, hydroxyarnino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

10

117. A benzodiazepine compound having the structure:



or its enantiomer,

wherein,

15 R₁ is an optionally substituted bisphenyl;

R₂ is aliphatic, aryl, -NH₂, or -NHC(=O)-R₅,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

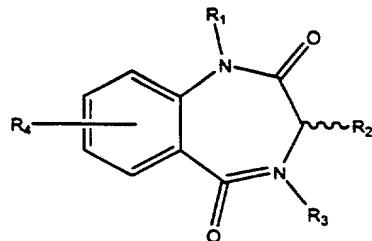
wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;

and

20 each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acetylarnino, hydroxyarnino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

118. A benzodiazepine compound having the structure:



or its enantiomer,

5 wherein,

R₁ is an optionally substituted bisphenyl;

R₂ is aliphatic, aryl, -NH₂, or -NHC(=O)-R₅,

wherein R₅ is aryl, heterocyclic, -R₆-NH-C(=O)-R₇ or -R₆-C(=O)-NH-R₇,

wherein R₆ is an aliphatic linker of 1-6 carbons and R₇ is aliphatic, aryl, or heterocyclic;

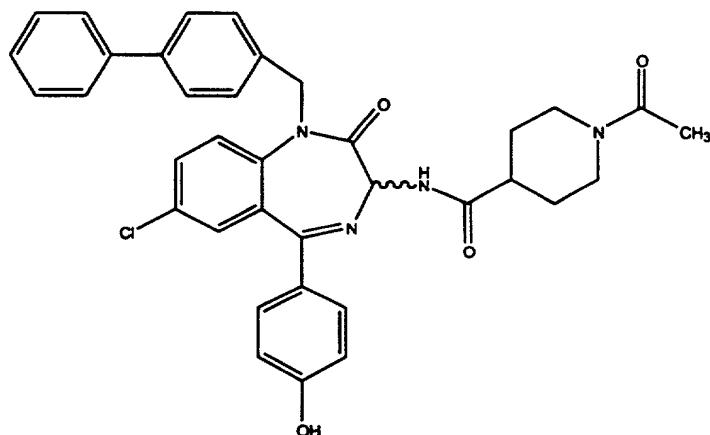
10 and

each of R₃ and R₄ is independently hydrogen, hydroxy, alkoxy, halo, amino, lower-alkyl-substituted-amino, acylamino, hydroxyamino, an aliphatic group having 1-8 carbons and 1-20 hydrogens, aryl, or heterocyclic;

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

15

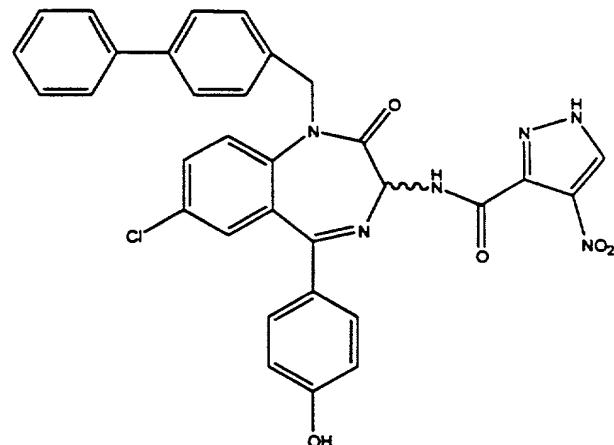
119. A compound having the structure:



or its enantiomer,

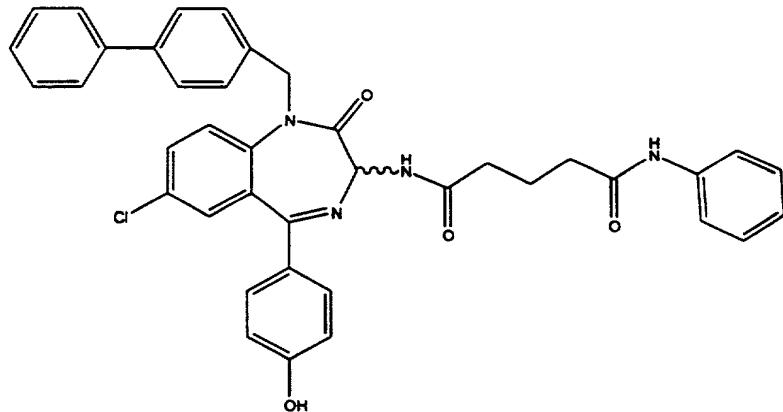
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

120. A compound having the structure:



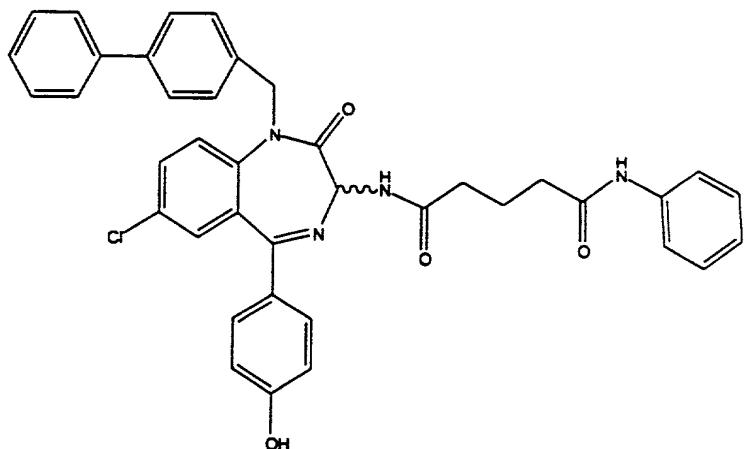
5
or its enantiomer,
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

121. A compound having the structure:



10
or its enantiomer,
or a pharmaceutically acceptable salt, prodrug or derivative thereof.

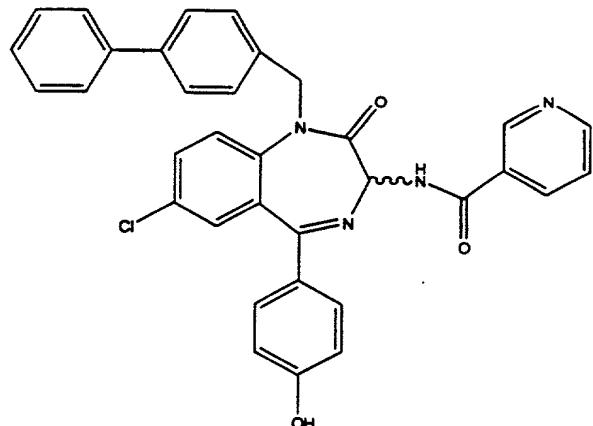
122. A compound having the structure:



or its enantiomer,

5 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

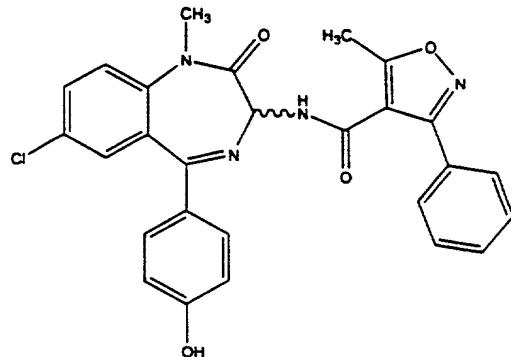
123. A compound having the structure:



or its enantiomer,

10 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

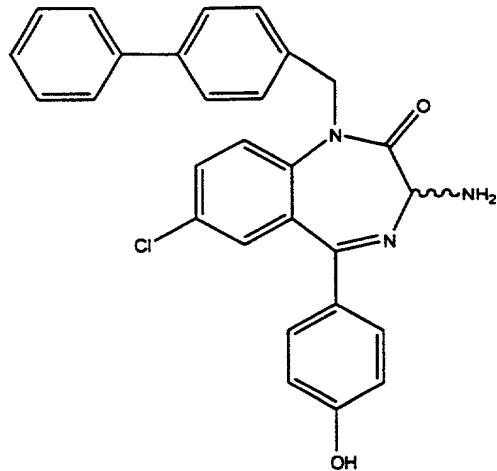
124. A compound having the structure:



or its enantiomer,

5 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

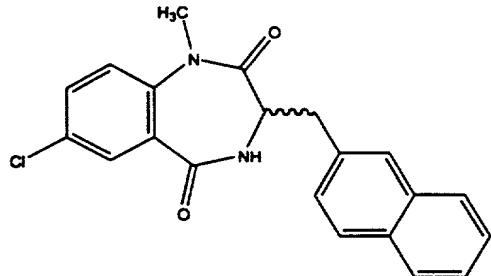
125. A compound having the structure:



or its enantiomer,

10 or a pharmaceutically acceptable salt, prodrug or derivative thereof.

126. A compound having the structure:



or its enantiomer,

or a pharmaceutically acceptable salt, prodrug or derivative thereof.

127. The method of claim 17, wherein the hyperproliferative disorder is neuroblastoma
5 or ovarian cancer.

128. The method of claim 49, wherein the hyperproliferative disorder is neuroblastoma
or ovarian cancer.

10 129. The method of claim 111, wherein the hyperproliferative disorder is neuroblastoma
or ovarian cancer.